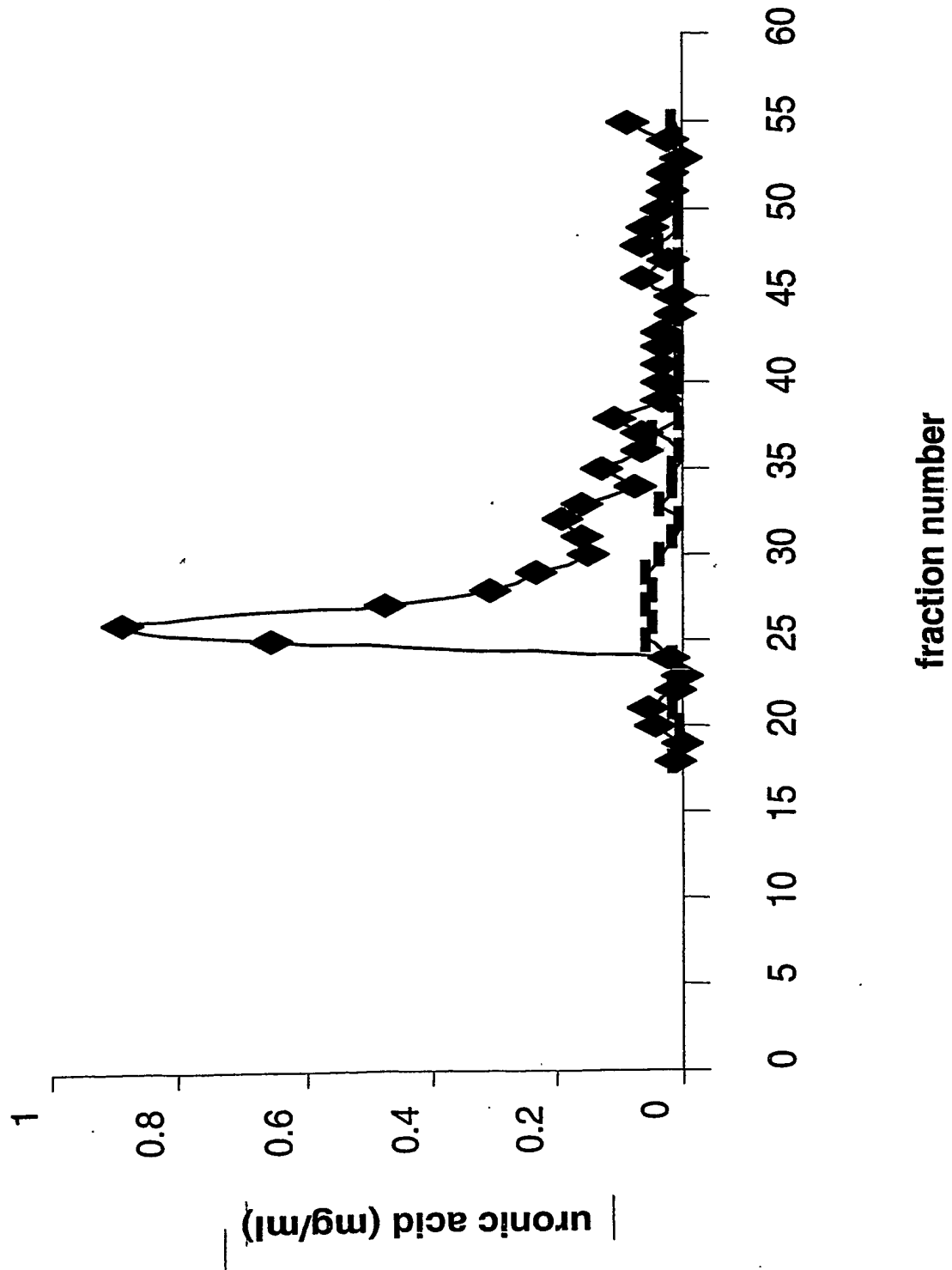


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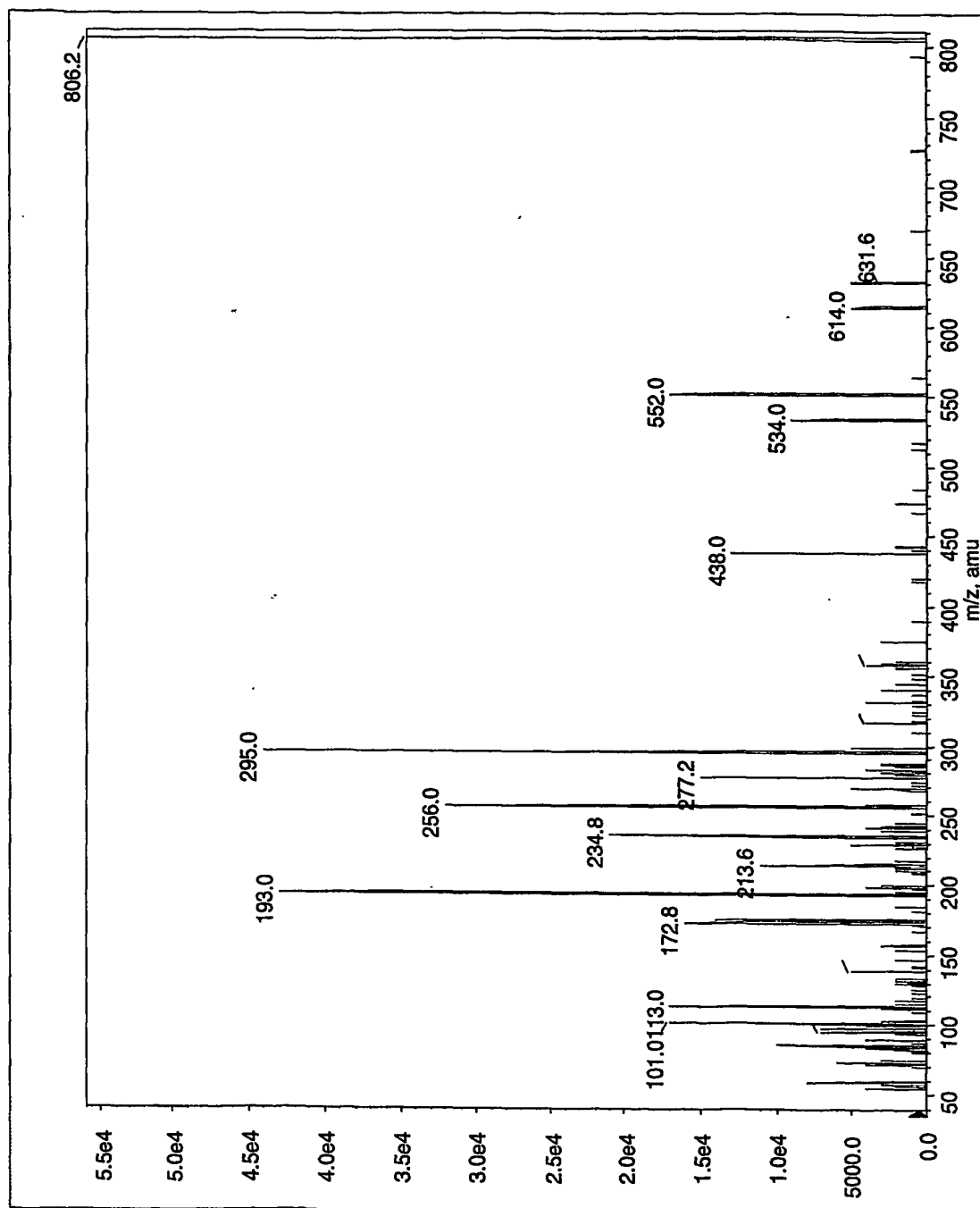


Figure 3 of 26

Oligosaccharide ^a	m/z	MRM pair	P2 fraction ^b	GAG ^c
IdoA- GalNAc4SQ-UA- GalNAc- UA (+SQ)	720	720/269	#31 and #32	DS
IdoA- GalNAc4SQ-UA- GalNAc (+SQ)	632	632/298	#34 and #35	DS
IdoA- GalNAc4SQ-UA	982	982/269	#38 and #39	DS
	490	490/173		
IdoA-HN-UA (+SQ)	940	940/269	#37	HS
IdoA-HN-UA (+2SQ)	1020	1020/940	#37	HS
	509	509/422		
IdoA- HNAc (+SQ)	806	806/295	#40 and #41	HS/DS

^a IdoA, iduronic acid; GalNAc, N-acetyl/galactosamine; GalNAc4SQN- acetyl/galactosamine
4 - sulfate; UA, uronic acid; HN, hexosamine; HNAc, N-acetyl/hexosamine.
^b fractions from the Bio- Gel P2 column (see Figure 23).
^c proposed source of oligosaccharide (DS, dermatan sulfate; HS, heparan sulfate).

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Figure 5 of 26

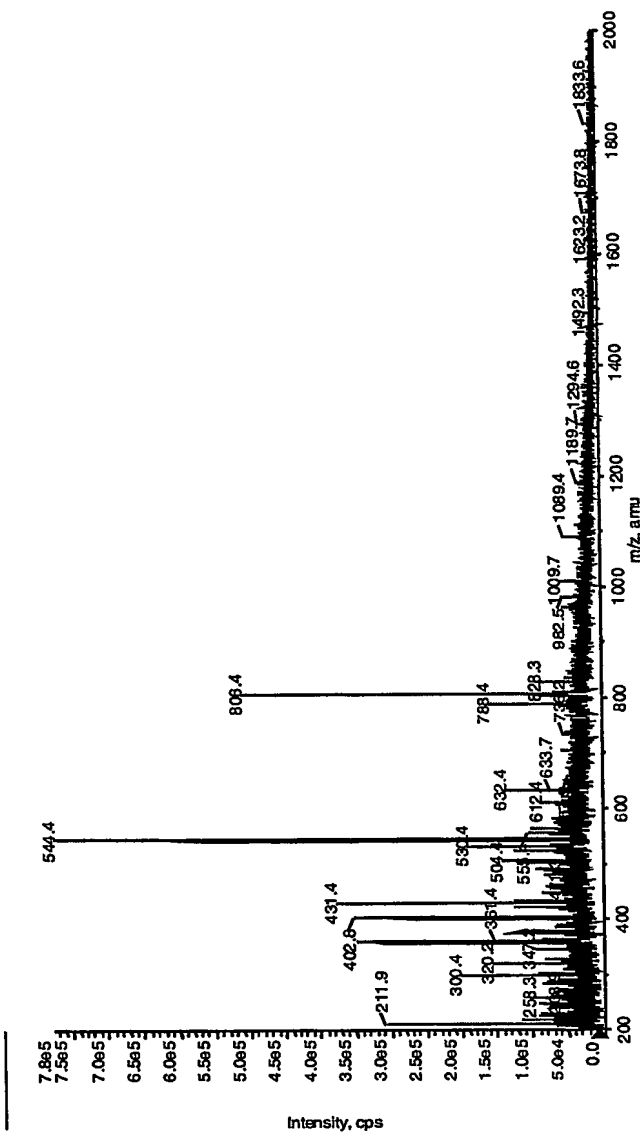
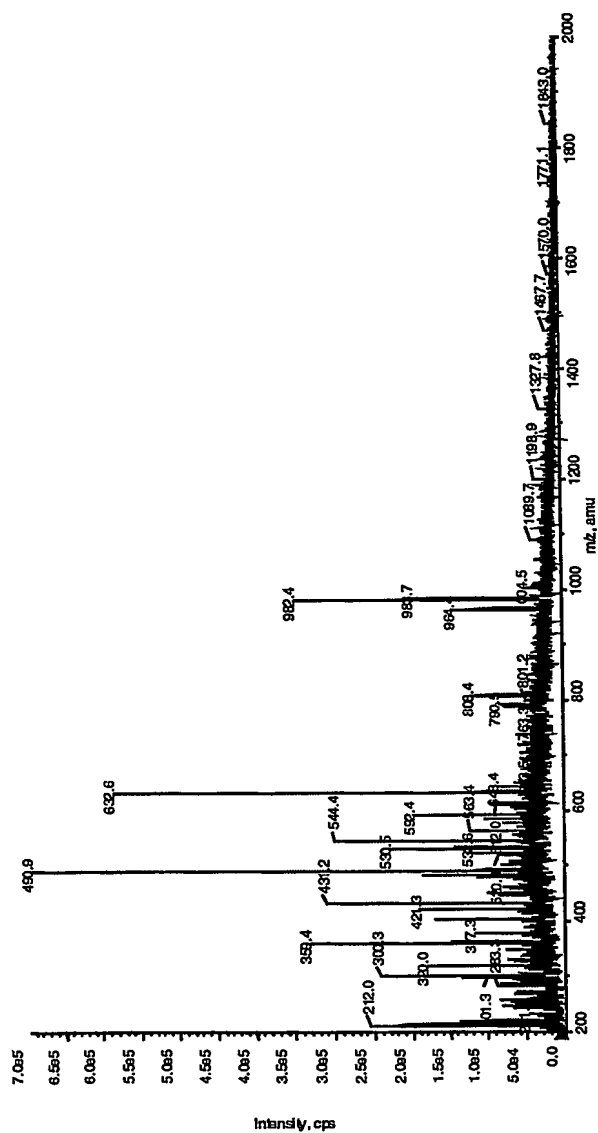
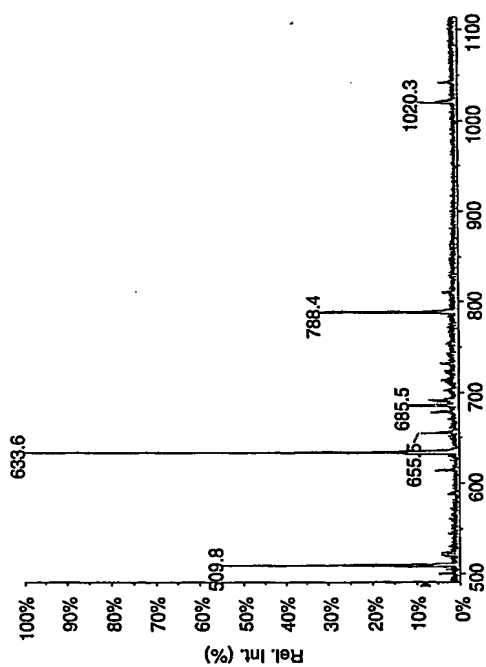


Figure 6 of 26

A



B

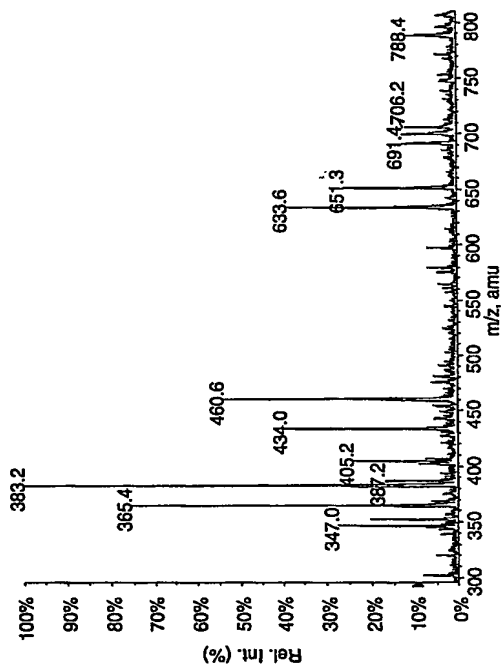


Figure 7 of 26

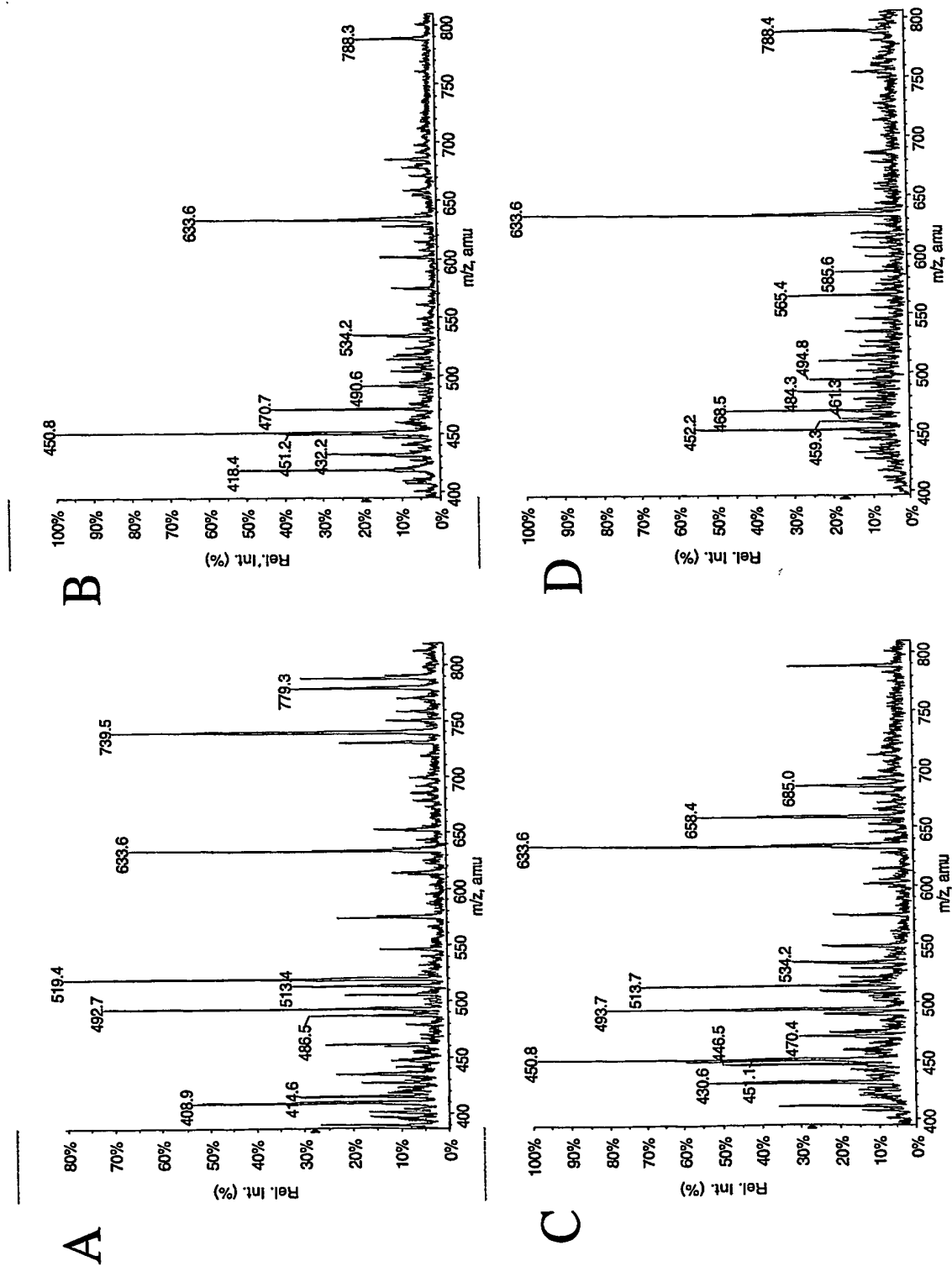


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Relative oligosaccharide levels in control^a urine

Oligosaccharide ^b	Q1/Q3 ^c	Average value ^d	Std. Dev.
UA	523/173	0.1480	0.1119
HNAC	550/173	0.0036	0.0028
HNACS	630/256	0.0016	0.0007
HNACS2	710/256	0.0030	0.0018
HNAC-UA	726/331	0.0155	0.0196
(HNAC, UA)	726/173	0.0063	0.0072
(HNS, UA)	764/173	0.0736	0.0295
HNS-UA	764/331	0.1148	0.1041
(HNAC, UA, S)	806/173	0.0003	0.0003
UA-HNACS	806/295	0.1941	0.1198
HNACS-UA	806/331	0.0999	0.0882
UA-HN-UA (S)	940/269	0.0294	0.0106
UA-HNAC-UA (S)	982/269	0.0111	0.0120
UA-HNAC-UA (S)	490/173	0.0045	0.0029
UA-HNAC-UA (S)	490/476	0.0305	0.0161
UA-HN-UA (S2)	1020/269	0.0026	0.0013
UA-HN-UA (S2)	1020/940	0.0018	0.0015
UA-HN-UA (S2)	509/422	0.0011	0.0018
HNAC-UA-HNAC (S2)	544/173	0.0507	0.0345
HNAC-UA-HNAC-UA (S)	1185/931	0.0099	0.0080
HNAC-UA-HNAC-UA (S)	591/173	0.2024	0.1818
HNAC-UA-HNAC-UA (S2)	632/298	0.0556	0.0358
UA-HNAC-UA-HNAC-UA (S2)	720/269	0.0024	0.0024
HNAC-UA-HNAC-UA-HNAC	734/173	0.0044	0.0027
HNAC-UA-HNAC-UA-HNAC (S3)	515/173	0.0291	0.0112
Unknown	528/448	0.0195	0.0082
Hexasaccharide	764/256	0.0007	0.0006

^a Controls = 26^b UA=uronic acid, HN=hexosamine, HNAC=N-acetylhexosamine, S=sulphate, structures in brackets indicate unknown sequence.^c m/z values used for the MRM analysis of selected oligosaccharides.^d values refer to the ratio values of the oligosaccharide signals to the internal standards GlcNAc6S (d3) (used for the monosaccharides) and the chondroitin disaccharide α -ΔUA-[1-3]-GalNAc-6S (used for disaccharides and larger species).

Figure 9 of 26

Mann Whitney U values for oligosaccharide analytes in MPS subgroups^d compared to controls^e

Oligosaccharide ^a	MPS I 15	MPS II 13	MPS IIIA 12	MPS IIIB 7	MPS IIIC 2	MPS IIID 2	MPS IVA 6	MPS VI 10	MS 1
UA	184	156.5	136	75	19.5 ^c	24.5	70	83	2
HNAC	128	123.5	99	79	40	26	53	106	5
HNACs	73 ^b	101 ^c	67 ^b	53	27	0 ^c	0 ^b	0 ^b	5.5
HNACs2	85 ^b	127	60 ^b	58	22	14	30 ^c	7 ^b	4
HNAC-UA	170.5	134.5	117	43 ^c	29	21	51	55 ^b	3
(HNAC, UA)	170	123	86 ^c	77	23.5	10	39	62 ^c	5
(HNS, UA)	5 ^b	4 ^b	31 ^b	49.5	25	1 ^c	32 ^c	104	0
HNS-UA	114.5 ^c	17 ^b	0 ^b	51	44.5	1 ^c	42	75.5	0
(HNAC, UA, S)	150	71.5 ^b	81.5 ^c	26 ^b	50	6	54	86	5
UA-HNACs	0 ^b	0 ^b	120.5	80	42	2 ^c	67	115	8
HNACs-UA	194	152	154	76	38	0 ^c	1 ^b	4 ^b	3
UA-HN-UA (S)	15.5 ^b	140	139.5	91	35.5	9	63	77	0
UA-HNAC-UA (S)	0 ^b	53 ^b	146	88	35	21	70.5	90	7
UA-HNAC-UA (S)	75.5 ^b	153	140	65	45	5	38	108	7
UA-HNAC-UA (S)	0 ^b	8 ^b	140	51	36	23	67.5	128	5
UA-HN-UA (S2)	169	52 ^b	66 ^b	40 ^c	7 ^b	21	37 ^c	48 ^b	9
UA-HN-UA (S2)	86.5 ^b	134	113.5	81	48	22	71	115	1
UA-HN-UA (S2)	24 ^b	136	69 ^b	76	46	22	75	96	0
HNAC-UA-HNAC (S2)	109 ^c	78 ^b	133.5	78	46	10	15.5 ^b	62 ^c	5
HNAC-UA-HNAC-UA (S)	0 ^b	134	64 ^b	0 ^b	22	3 ^c	10 ^b	29 ^b	0
HNAC-UA-HNAC-UA (S)	61 ^b	68 ^b	128	34 ^c	37	11	56	118.5	13
HNAC-UA-HNAC-UA (S2)	5 ^b	130	31 ^b	5 ^b	28	0 ^c	10.5 ^b	0 ^b	0
UA-HNAC-UA-HNAC-UA (S2)	61.5 ^b	131	101.5	71.5	31	8	70	122.5	2
HNAC-UA-HNAC-UA-HNAC	188	76.5 ^b	90 ^c	63	27	17	50	108	4
HNAC-UA-HNAC-UA-HNAC (S3)	167	55.5 ^b	125	44.5 ^c	50	17	68	105	11
Unknown (528/448)	60.5 ^b	54 ^b	43 ^b	57	24	8.5	41	110	2
Hexasaccharide (764/256)	0 ^b	0 ^b	13 ^b	1 ^b	3 ^b	0 ^c	2 ^b	8 ^b	0

^a UA=uronic acid, HN=hexosamine, HNAC=N-acetylhexosamine, S=sulphate, structures in brackets indicate unknown sequence.^b p<0.01^c p<0.5^d MPS types are shown with the number of patient samples below

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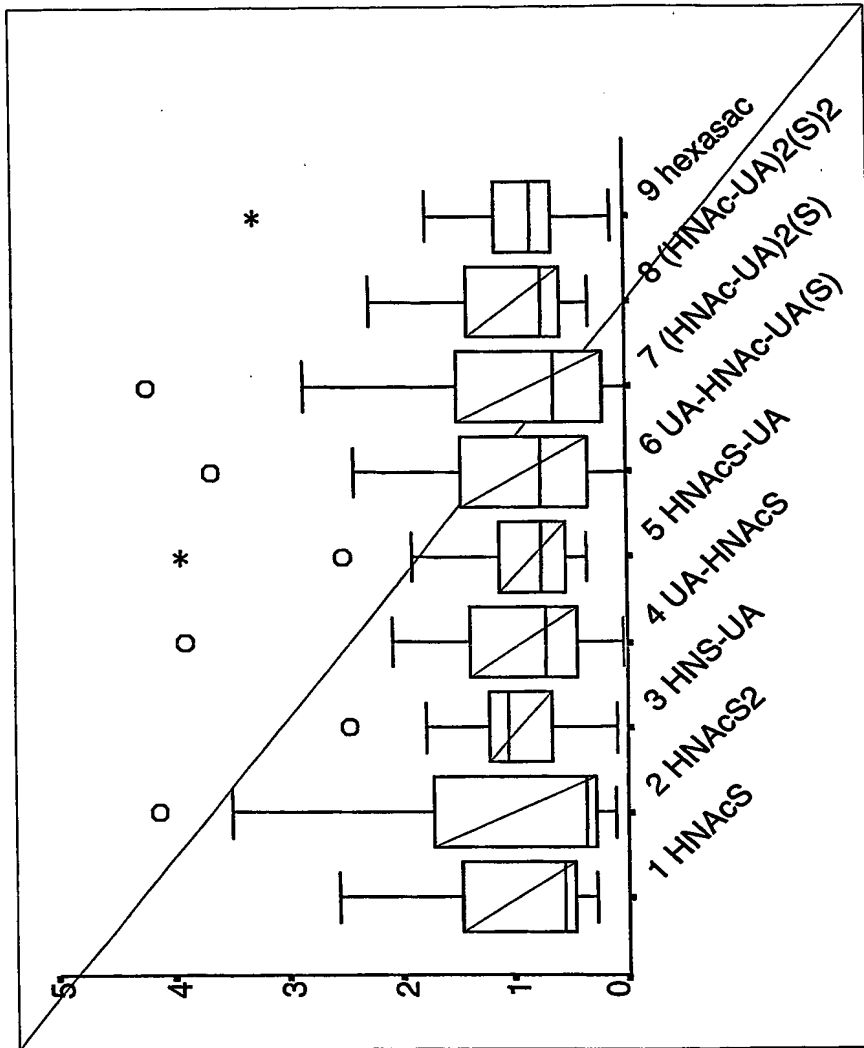
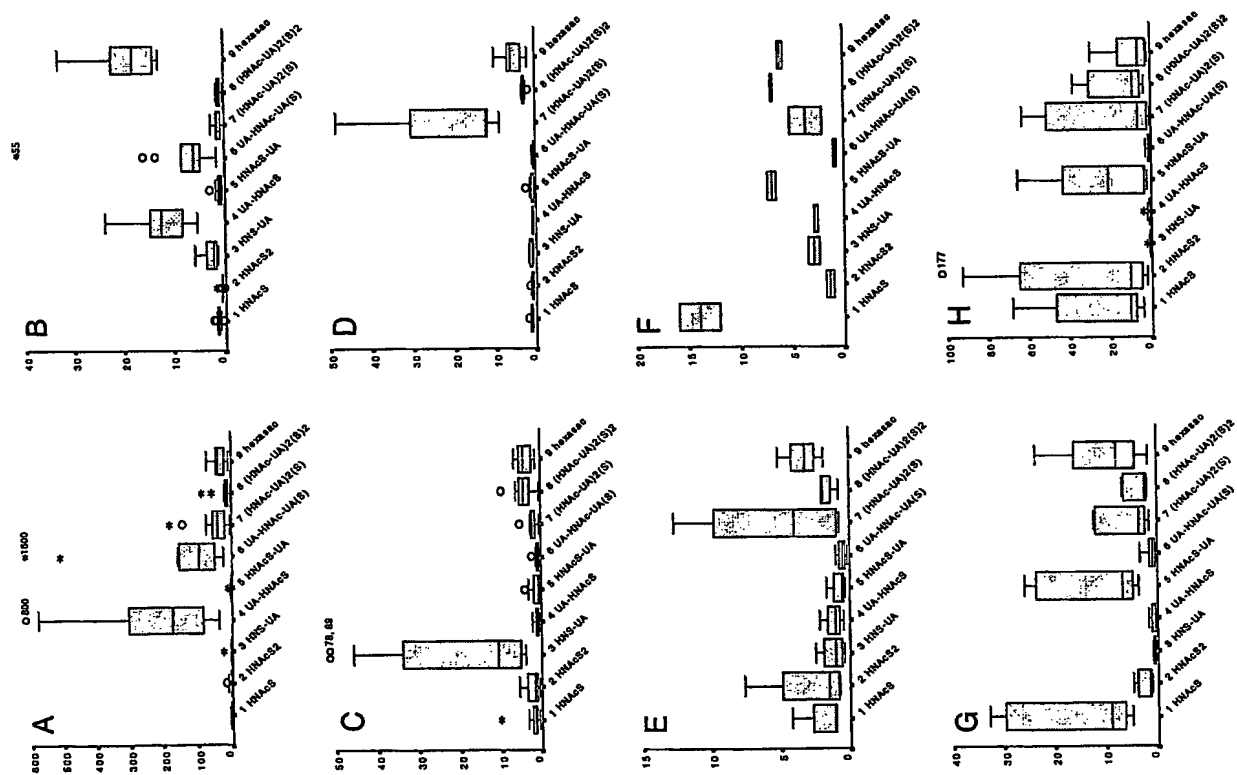


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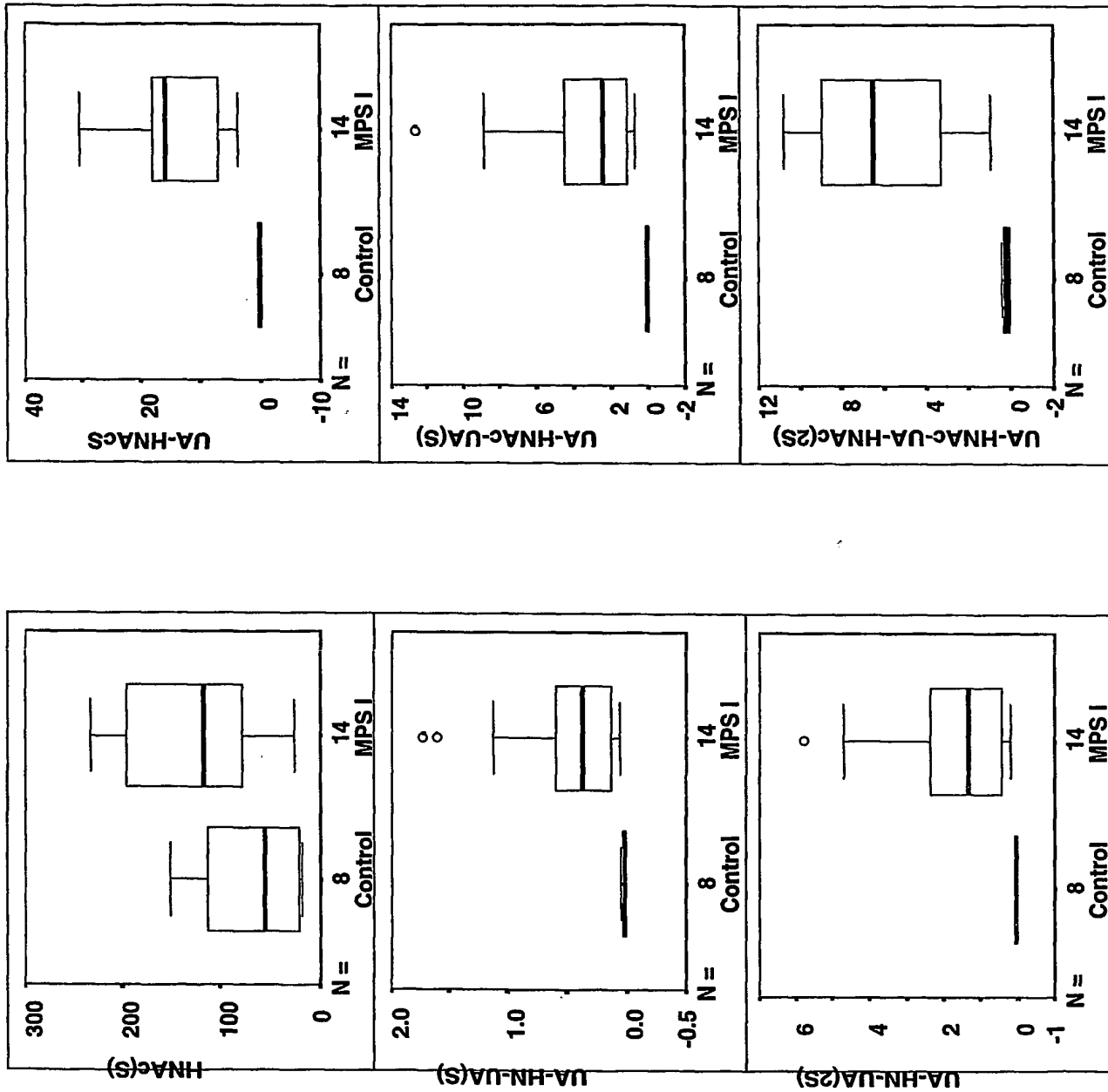


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Cell line	Disorder	UA-HN-UA(Sx2) ¹
SF 5344	Control	0.034
SF 5248	Control	0.030
SF 2662	MPS I (intermediate)	0.090
SF 5048	MPS I (severe)	0.379
SF 538	MPS I (severe)	0.387

¹ relative level of oligosaccharide/mg cell protein

UA = uronic acid; HN = hexosamine

Figure 14 of 26

Genotype	632/298 (MRM)	982/269 (MRM)	940/269 (MRM)	1020/269 (MRM)	509/422 (MRM)	806/295 (MRM)
W402Xhom	30.8	93.6	14.0	4.8	20.0	111.8
W402X, Q70X	5.4	10.9	1.0	3.3	1.0	51.4
W180X, c134-145del	5.6	5.7	0.55	0.69	1.6	25.2
P533R, W402X	4.4	5.7	0.67	0.32	1.1	40.9
R89Q, 1060+2t>c	3.4	2.7	0.13	0.33	0.89	11.3
R89Q, 1060+2t>c	5.4	2.2	0.19	0.19	1.0	10.5
L346R, c704ins5	2.7	1.5	0.21	0.18	0.68	9.1
Control range (n=26)	0.07-0.9	0.07-0.6	0.02-0.2	0-4.0	0-0.6	0.03-0.5

Figure 15 of 26

Oligosaccharide ¹ MRM pairs	Pre-BMT	Post-BMT (3 months)	Post-BMT (8 months)	Control Avg (n=8)	Control Std Dev
UA-HN-UA(Sx2)	509/422	2.31	0.63	0.59	0.05
HNAc(S)	630/256	192	165	139	68
UA-HNAc(S)	806/295	13.93	8.39	2.12	0.04
UA-HN-UA(S)	940/269	0.49	0.21	0.19	0.03
UA-HNAc-UA(S)	982/269	2.58	1.86	1.05	0.06
UA(S)					
UA-HNAc-UA-HNAc(Sx2)	632/298	9.34	4.51	2.57	0.23
					0.16

¹ UA = uronic acid; HN = hexosamine; S = sulphate; HNAc = N-acetylhexosamine

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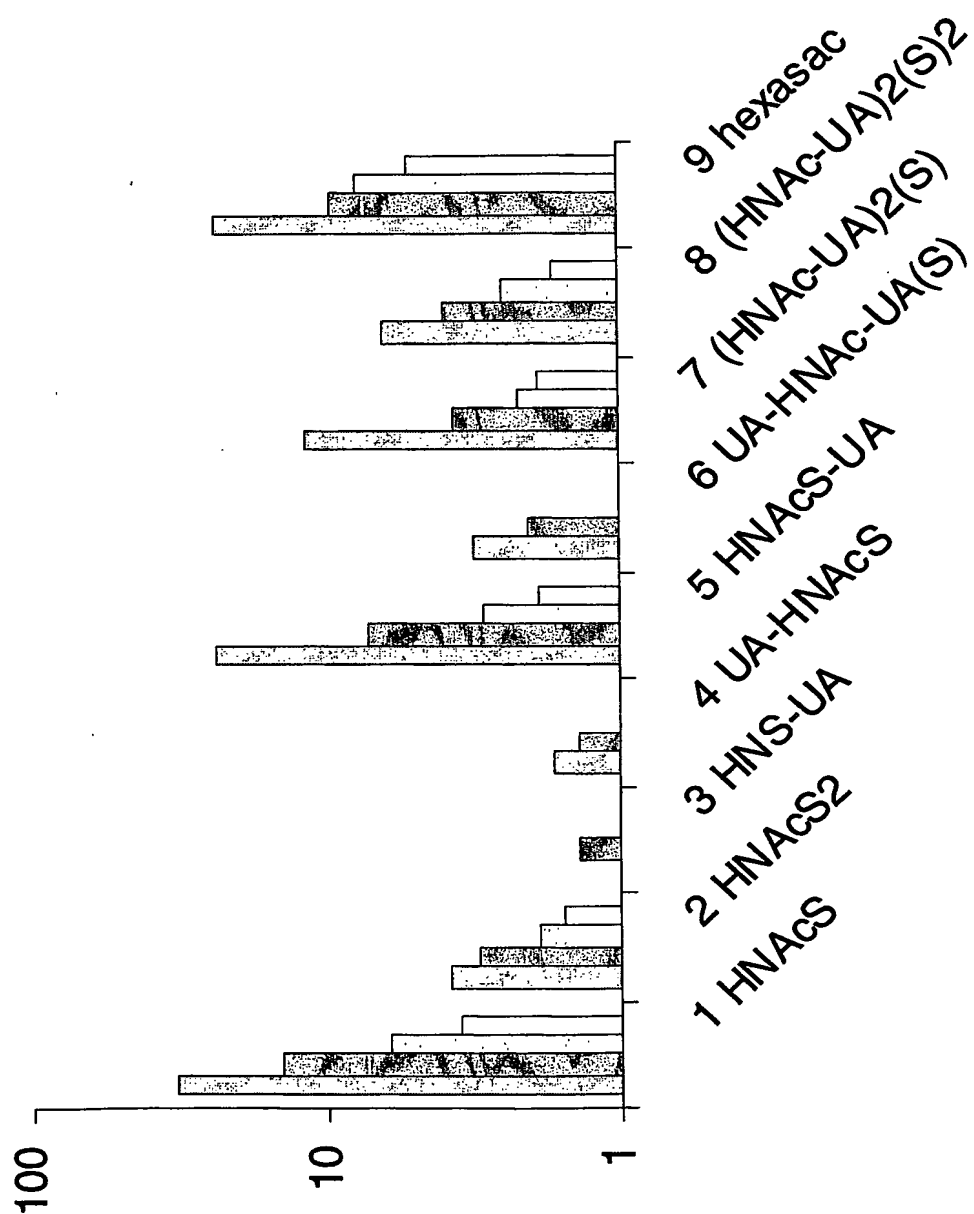


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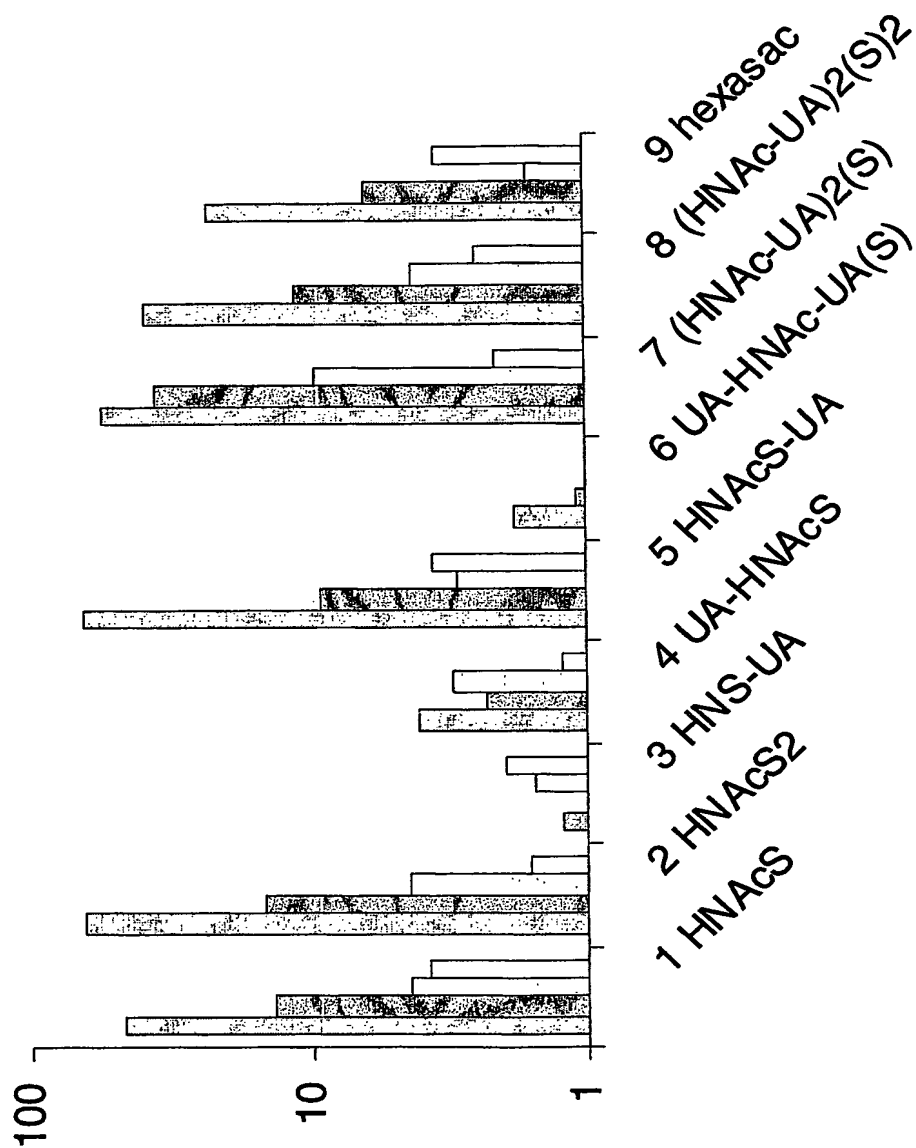


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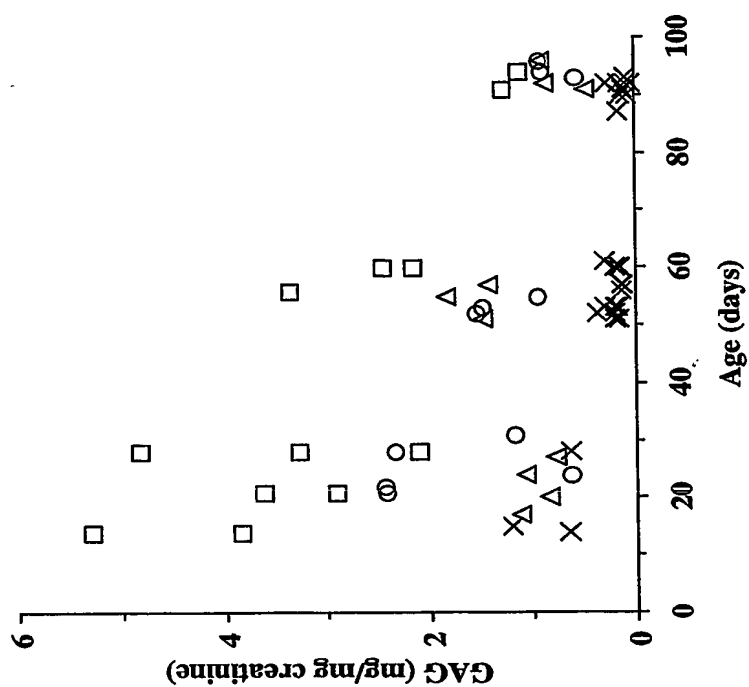


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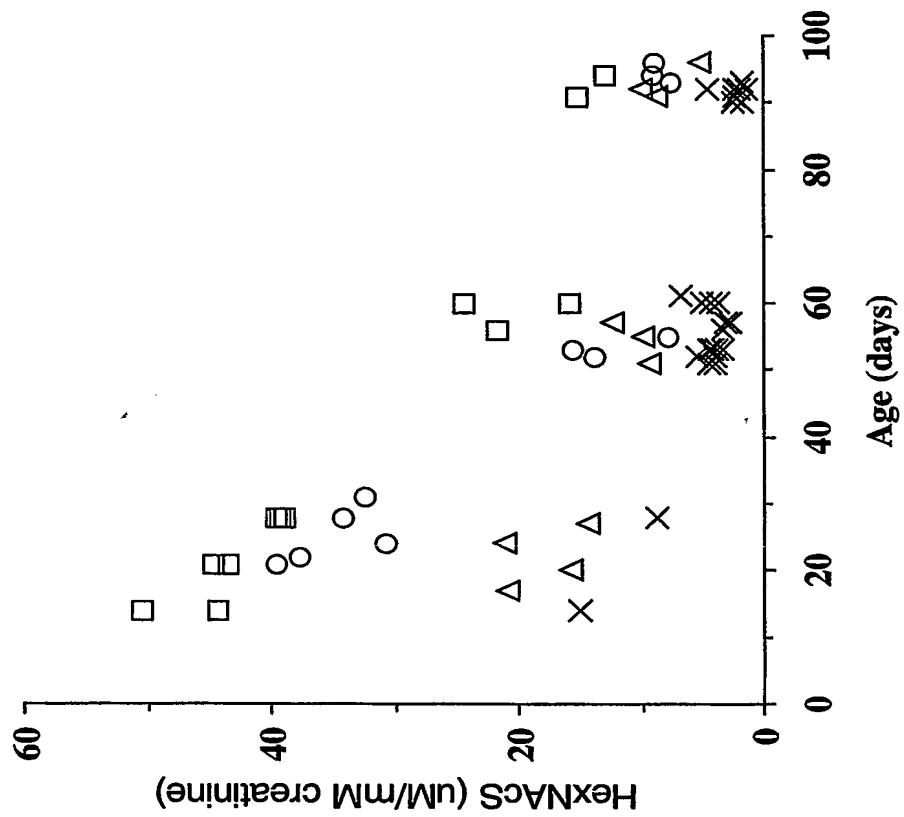


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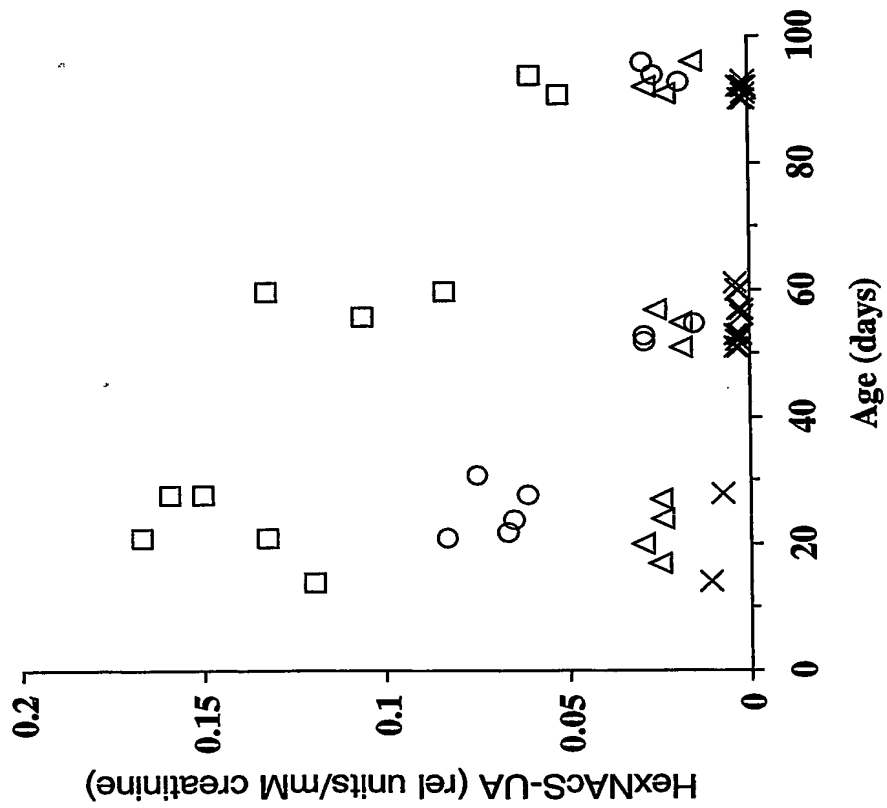


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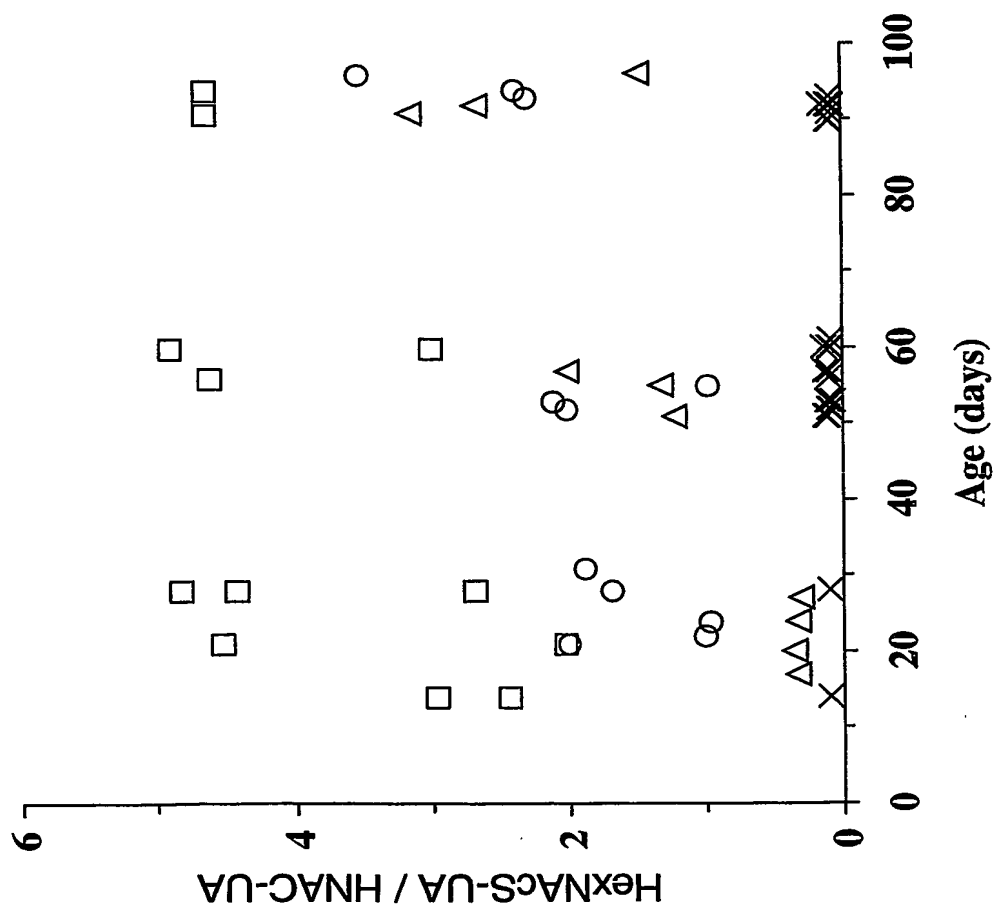


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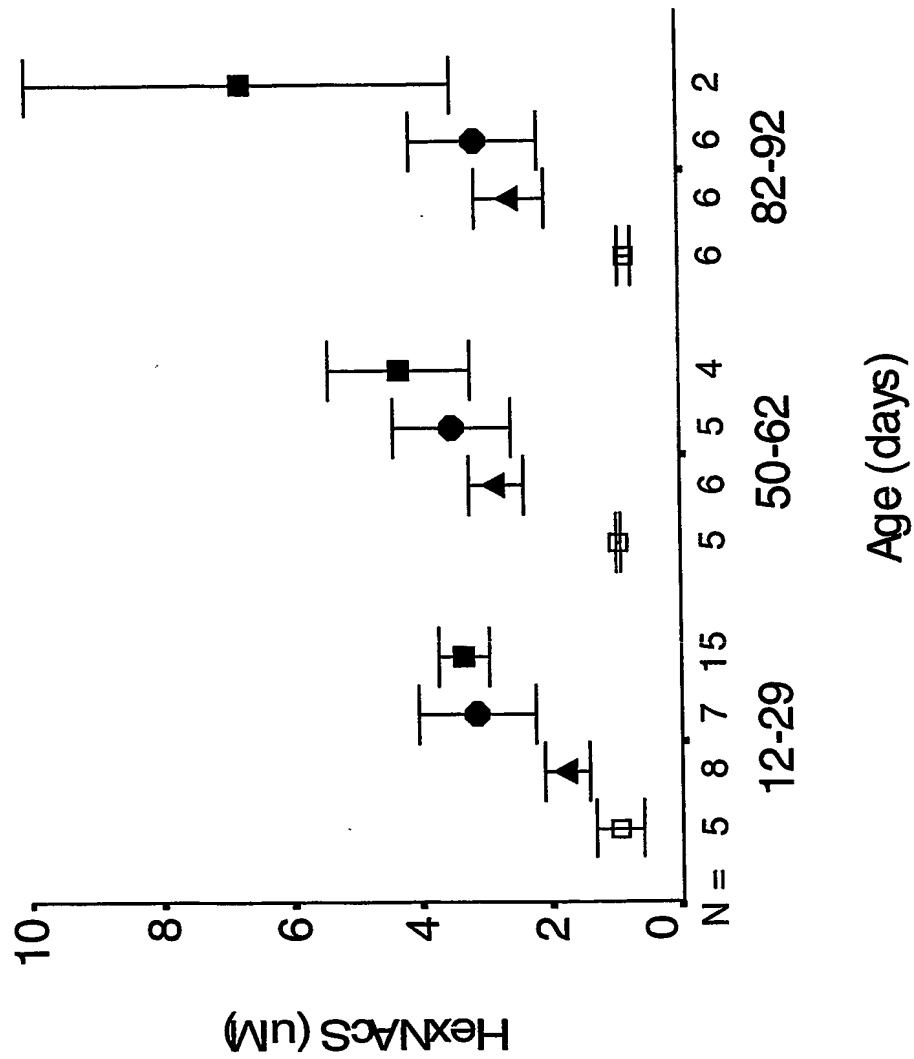


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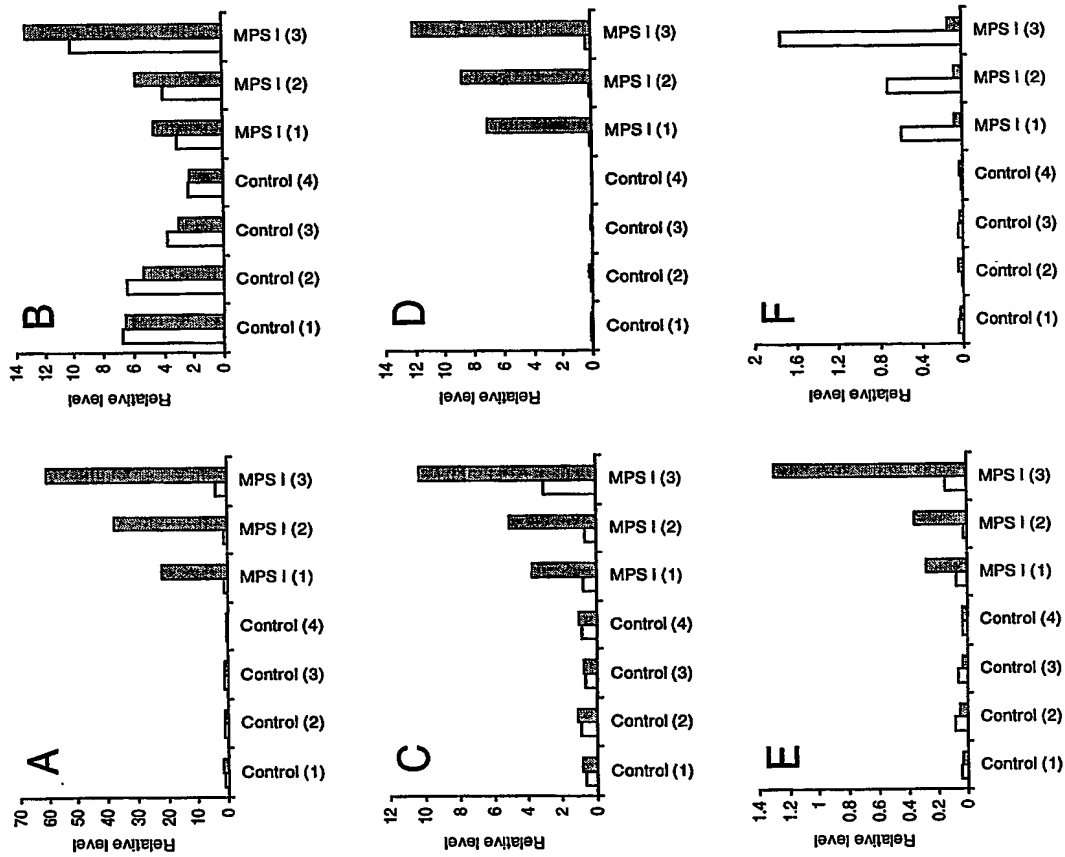


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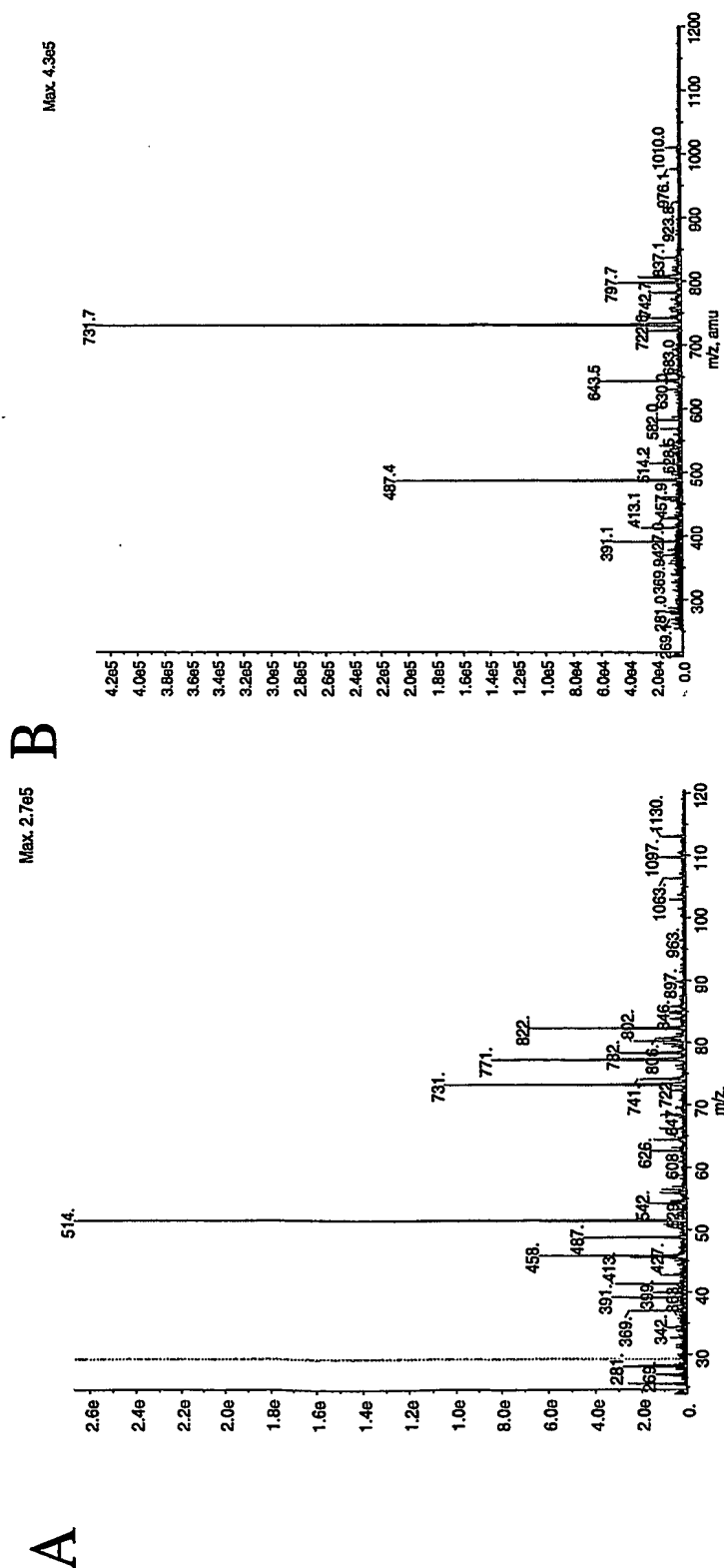


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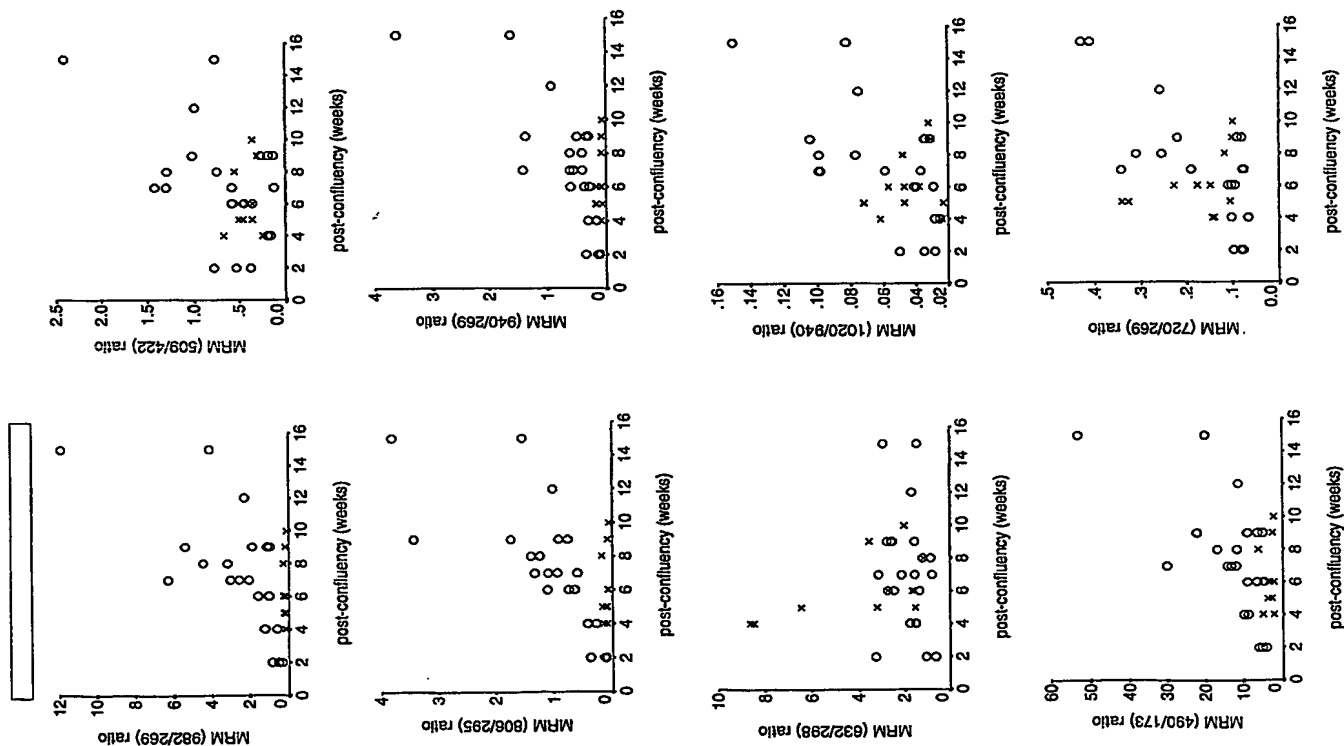
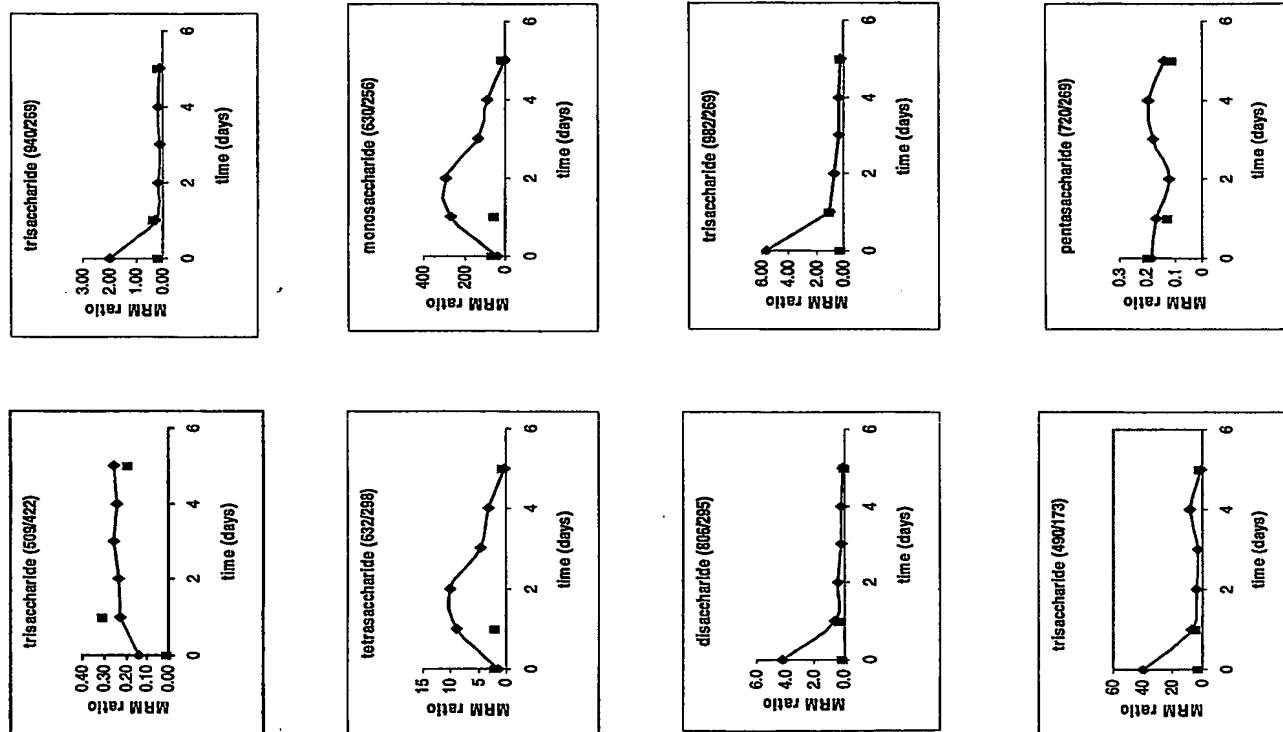


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